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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : Moses Rodriguez and Daren Ure

U.S. Serial No.: 09/885,227 Examiner: Not Yet Known

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For : TREATMENT OF CENTRAL NERVOUS SYSTEM DISEASES BY ANTIBODIES AGAINST GLATIRAMER ACETATE

1185 Avenue of the Americas
New York, New York 10036
October 18, 2002



Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

**INFORMATION DISCLOSURE STATEMENT**
**PURSUANT TO 37 C.F.R. §1.97(b)(3)**

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following Reference Items 1-164 **(Exhibits 1-154)** which are listed again on the accompanying Form PTO 1449 **(Exhibit A)**. Applicants request that the Examiner review the publications and make them of record in the subject application.

This Information Disclosure Statement is being submitted before the issuance of a first Office Action on the merits in connection with the subject application. Accordingly, no fee is required and this Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(b)(3).

For the convenience of the Examiner, applicants point out that Reference Items 102, 126, and 155 were cited in the November 19, 2001 International Search Report in the corresponding PCT International application, and a copy of the Report is enclosed as **Exhibit B**.

Applicants also point out that several of the listed references are counterparts of each other and are cumulative. Therefore, in accordance with 37 C.F.R. § 1.98(c), a counterpart of a reference is identified after the cite to the reference, but a copy of only one of the counterparts is being provided. Applicants will provide the Examiner with copies of any reference upon request.

1. U.S. Patent No. 3,849,550, issued November 19, 1974 (Teitelbaum, et al.) **(Exhibit 1)**;

2. U.S. Patent No. 4,339,431, issued July 13, 1982 (Gaffar) **(Exhibit 2)**;

3. U.S. Patent No. 5,204,099, issued April 20, 1993 (Barbier, et al.) **(Exhibit 3)**;

4. U.S. Patent No. 5,591,629, issued January 7, 1997 (Rodriguez et al.) **(Exhibit 4)**;

5. U.S. Patent No. 5,627,206, issued May 6, 1997 (Hupe, et al.) **(Exhibit 5)**;

6. U.S. Patent No. 5,668,117, issued September 16, 1997 (Shapiro) **(Exhibit 6)**;

7. U.S. Patent No. 5,719,296, issued February 17, 1998 (Acton, III, et al.) **(Exhibit 7)**;

8. U.S. Patent No. 5,800,808, issued September 1, 1998 (Konfino, et al.) **(Exhibit 8)**;

9. U.S. Patent No. 5,858,964, issued January 12, 1999 (Aharoni, et al.) **(Exhibit 9)**;

10. U.S. Patent No. 5,981,589, issued November 9, 1999 (Konfino, et al.) **(Exhibit 10)**;

11. U.S. Patent No. 5,958,972, issued September 28, 1999 (Hupe, et al.) **(Exhibit 11)**;

12. U.S. Patent No. 6,048,898, issued April 11, 2000 (Konfino, et al.) **(Exhibit 12)**;

13. U.S. Patent No. 6,054,430, issued April 25, 2000 (Konfino, et al.) **(Exhibit 13)**;

14. U.S. Patent No. 6,214,791, issued April 10, 2001 (Arnon, et al.) **(Exhibit 14)**;

15. U.S. Patent No. 6,342,476, issued January 29, 2002 (Konfino, et al.) **(Exhibit 15)**;

16. U.S. Patent Publication No. US-2001-0055568-A1, published December 27, 2001 (Gilbert et al.) **(Exhibit 16)**;

17. U.S. Serial No. 09/359,099, filed July 12, 1999 (Strominger et al.) **(Exhibit 17)**;

18. U.S. Serial No. 09/405,743, filed September 24, 1999 (Gad et al.) **(Exhibit 18)**;

19. U.S. Serial No. 09/768,872, filed January 23, 2001, (Aharoni et al.)**(Exhibit 19)**;

20. U.S. Serial No. 09/816,989, filed March 23, 2001 (Gad et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/405,743 (Exhibit 18);

21. PCT International Publication No. WO 88/10120 (PCT/US88/02139), published December 29, 1988 (Weiner, et al.)**(Exhibit 20)**;

22. PCT International Publication No. WO 95/31990 (PCT/US95/06551), published November 30, 1995 (Konfino, et al.) Applicants point out that this reference is a counterpart of U.S. Patents Nos. 5,800,808 (Exhibit 8) and 6,342,476 (Exhibit 15);

23. PCT International Publication No. WO 95/33475 (PCT/EP95/02125), published December 14, 1995 (Kott, et al.) **(Exhibit 21)**;

24. PCT International Publication No. WO 98/30227 (PCT/US98/00375), published July 16, 1998 (Arnon et al.). Applicants point out that this reference is a counterpart of US Patent No. 6,214,791 (Exhibit 14);

25. PCT International Publication No. WO 00/05250 (PCT/US99/16747) published February 3, 2000 (Aharoni et al.). Applicants point out that this reference is a counterpart of US Serial No. 09/768,872 (Exhibit 19);

26. PCT International Publication No. WO 00/18794 (PCT/US99/22402) published April 6, 2000 (Gad, et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/405,743 (Exhibit 18) and U.S. Serial No. 09/816,989;

27. PCT International Publication No. WO 00/20010 (PCT/US99/22836), published April 13, 2000 (Flechter et al.)**(Exhibit 22)**;

28. PCT International Publication No. WO 00/27417 (PCT/US99/27107), published May 18, 2000 (Aharoni et al.)**(Exhibit 23)**;

29. PCT International Publication No. WO 00/05249 (PCT/US99/16617), published February 3, 2000 (Strominger et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/359,099 (Exhibit 17);

30. PCT International Publication No. WO 01/85797 (PCT/US00/14902), published November 15, 2001 (Rodriguez et al.)**(Exhibit 24)**;

31. PCT International Publication No. WO 01/60392 (PCT/US01/05198), published August 23, 2001 (Gilbert et al.). Applicants point out that this reference is a counterpart of US Patent Publication No. US-2001-0055568-A1 (Exhibit 16);

32. PCT International Publication No. WO 01/93828 (PCT/US01/18248), published December 13, 2001 (Yong and

Chabot). Applicants point out that this reference is a counterpart of U.S. Serial No. 875,429 (Exhibit 20);

33. PCT International Publication No. WO 01/97846 (PCT/US01/19649), published December 27, 2001 (Rodriguez and Ure). Applicants point out that this reference is a counterpart of the subject application;

34. European Patent Application No. 0 383 620 A2, published August 22, 1990 (Cook) **(Exhibit 25)**;

35. European Patent No. 0 359 783 B1, published November 29, 1995 (Weiner, et al.). Applicants point out that this reference is a counterpart of PCT International Application No. PCT/US88/02139 (WO 88/10120)(Exhibit 21);

36. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Polypeptide", Israel J. Med. Sci., 1971, 7, 630-631 (Abstract) **(Exhibit 26)**;

37. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Polypeptide", Eur. J. Immunol., 1971, 1, 242-248 **(Exhibit 27)**;

38. Arnon, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Copolymer Immunological Cross Reactive with Basic Encephalitogen", Israel J. Med. Sci., 1972, 8, 1759-1760 **(Exhibit 28)**;

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40. Webb, et al., "Further Studies on the Suppression of Experimental Allergic Encephalomyelitis by Synthetic Copolymer", Israel J. Med. Sci., 1972, 8, 656-657 **(Exhibit 30)**;

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45. Webb, et al., "Suppression of Experimental Allergic Encephalomyelitis in Rhesus Monkeys by a Synthetic Basic Copolymer", Isr. J. Med. Sci., 1975, 11, 1388 (Abstract) **(Exhibit 35)**;

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47. Abramsky, et al., "Effect of a Synthetic Polypeptide (COP-1) on Patients with Multiple Sclerosis and with Acute Disseminated Encephalomyelitis", J. Neurol. Sci., 1977, 31, 433-438 **(Exhibit 37)**;

48. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis in Baboons by Cop 1", Israel J. Med. Sci., 1977, 13, 1038 (Abstract) **(Exhibit 38)**;

49. Arnon, et al., "Suppression of EAE in Baboons by a Synthetic Polymer of Amino Acids", Neurol., 1978, 28, 336 (Abstract) **(Exhibit 39)**;

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53. Lando, et al., "Effect of Cyclophosphamide on Suppressor Cell Activity in Mice Unresponsive to EAE", J. Immunol., 1979, 123, 2156-2160 (Abstract) **(Exhibit 43);**

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58. Arnon, "A Synthetic Copolymer of Amino Acids in a Clinical Trial for MS Therapy" in Progress in Multiple Sclerosis

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65. Lisak, et al., "Effect of Treatment with Copolymer 1 (Cop-1) on the in Vivo and in Vitro Manifestations of Experimental Allergic Encephalomyelitis (EAE)", J. Neurol. Sci., 1983, 62, 281-293 **(Exhibit 55)**;

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68. Brosnan, et al., "Copolymer 1: Effect on Normal Human Lymphocytes", Ann. N.Y. Acad. Sci. (USA), 1984, 436, 498-499 **(Exhibit 58)**;

69. Bornstein, et al., "Multiple Sclerosis: Clinical Trials of a Synthetic Polypeptide, Copolymer 1", Neurol., 1985, 35 (Suppl. 1), 103 (Abstract) **(Exhibit 59)**;

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71. Burns, et al., "Human Cellular Immune Response in Vitro to Copolymer 1 and Myelin Basic Protein (MBP)", Neurol., 1985, 35 (Suppl. 1), 170 (Abstract) **(Exhibit 61)**;

72. Teitelbaum, et al., "Monoclonal Antibodies to Myelin Basic Protein Cross React with Synthetic EAE-suppressive Copolymer, COP 1" in Proc. 7th Eur. Immunol. Mtg., Jerusalem, September 8-13, 1985 (Abstract) **(Exhibit 62)**;

73. Thompson, "MCQ Tutor: Medical Immunology Multiple Choice Questions", Immunol. Today, 1985, 6(4), 141 **(Exhibit 63)**;

74. Burns, et al., "Human Cellular Immune Response to Copolymer 1 and Myelin Basic Protein", Neurol., 1986, 36, 92-94 **(Exhibit 64)**;

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76. Bornstein, et al., "A Pilot Trial of Cop 1 in Exacerbating-remitting Multiple Sclerosis", New Eng. J. Med., 1987, 317(7), 408-414 **(Exhibit 66)**;

77. Rolak, "Copolymer-I Therapy for Multiple Sclerosis", Clin. Neuropharmacology, 1987, 10(5), 389-396 **(Exhibit 67)**;

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82. Teitelbaum, et al., "Specific Inhibition of the T-cell Response to Myelin Basic Protein by the Synthetic Copolymer Cop 1", Proc. Natl. Acad. Sci. USA, 1988, 85, 9724-9728 **(Exhibit 72)**;

83. Arnon, et al., "Suppression of Experimental Allergic Encephalomyelitis by Cop-1 - Relevance to Multiple Sclerosis", Israel J. Med. Sci., 1989, 25, 686-689 **(Exhibit 73)**;

84. Bornstein, et al., "Pilot Trial of COP-1 in Chronic Progressive Multiple Sclerosis: Preliminary Report", from The International Multiple Sclerosis Conference: An Update on Multiple Sclerosis, Roma (Italy), September 15-17, 1988, in Elsevier Science Publisher, 1989, 225-232 **(Exhibit 74)**;

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94. Wender, "Copolymer 1 (COP-1) in the Treatment of Multiple Sclerosis (letter)" Neur. Neurochir. Pol., 1990, 24, 113 **(Exhibit 84)**;

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96. Burns, et al., "Failure of Copolymer 1 to Inhibit the Human T-cell Response to Myelin Basic Protein", Neurol., 1991, 41, 1317-1319 **(Exhibit 86)**;

97. Clinical Trial Protocol No. 9001, Teva Pharmaceutical Industries, Ltd., first patient enrolled October 23, 1991 **(Exhibit 87)**;

98. Ferrara, et al., "Graft-Versus-Host Disease", New Eng. J. Med., 1991, 324, 667-674 **(Exhibit 88)**;

99. Meiner, "COP-1 Multicenter Clinical Trial in Exacerbating-remitting Multiple-Sclerosis: One Year Follow-up", J. Neurol., 1991(Suppl. 1) (Abstract) **(Exhibit 89)**;

100. Rothbard, et al., "Interactions Between Immunogenic Peptides and MHC Proteins", Ann. Rev. Immunol., 1991, 9, 527-565 **(Exhibit 90)**;

101. Salvetti, et al., "Myelin Basic Protein T Cell Epitopes in Patients with Multiple Sclerosis", Department of Neurological Sciences, University of Rome, La Sapienza 1991, 72 (Abstract) **(Exhibit 91)**;

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103. Van den Bogaerde, et al., "Induction of Long-Term Survival of Hamster Heart Xenografts in Rats", Transplantation, 1991, 52, 15-20 **(Exhibit 93)**;

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105. Johnson, "Clinical Studies in Copolymer 1 Therapy for Exacerbating-remitting Multiple Sclerosis", in Congress for Advances in the Understanding and Treatment of Multiple Sclerosis, Boston (USA), Oct. 28-29, 1992 **(Exhibit 95)**;

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108. Teitelbaum, et al., "Synthetic Copolymer 1 Inhibits Human T-cell Lines Specific for Myelin Basic Protein", Proc. Natl. Acad. Sci. (USA), 1992, 89, 137-141 **(Exhibit 98)**;

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110. Aharoni, et al., "T Suppressor Hybridomas and Interleukin-2-Dependent Lines Induced by Copolymer 1 or by Spinal Cord Homogenate Down-Regulate Experimental Allergic Encephalomyelitis", Eur. J. Immunol., 1993, 23, 17-25 **(Exhibit 100)**;

111. Arnon, et al., "Immunomodulation of Experimental Allergic Encephalomyelitis", Israel J. Med. Sci., 1993, 29, 175-181 **(Exhibit 101)**;

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114. Francis, "The Current Therapy of Multiple Sclerosis", J. Clin. Pharmacy and Therapeutics, 1993, 18, 77-84 **(Exhibit 104)**;

115. Keleman, et al., "Graft-versus-Host Disease in Bone Marrow Transplantation: Experimental, Laboratory, and Clinical Contributions of the Last Few Years", Int. Arch. Allergy Immunol., 1993, 102, 309-320 **(Exhibit 105)**;

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in Exacerbating-remitting Multiple Sclerosis - Two-year Follow-up", in 9th Congress of the European Committee for Treatment and Research in Multiple Sclerosis, Florence (Italy), October-November, 1993, 48 (Abstract) **(Exhibit 107)**;

118. Milo, et al., "Copolymer-1 (COP-1) Regulates Class II MHC Expression and Cytokine Synthesis in the THP-1 Monocyte-Macrophage Cell Line" in The IBC Conference on Multiple Sclerosis, San Diego (USA), December 10, 1993 (Abstract) **(Exhibit 108)**;

119. Sela, "Polymeric Drugs as Immunomodulatory Vaccines Against Multiple Sclerosis", Makromol. Chem. Macromol. Symp., 1993, 70/71, 147-155 **(Exhibit 109)**;

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124. Dorling, et al., "Prospects for Xenografting", Curr. Opinions Immunol., 1994, 6, 765-769 **(Exhibit 114)**;

125. Fridkis-Hareli, et al., "Copolymer 1 Displaces MBP, PLP and MOG, but Can Not be Displaced by these Antigens from the MHC Class II Binding Site", Department of Chemical Immunology, The Weizmann Institute of Science, 1994 **(Exhibit 115)**;

126. Fridkis-Hareli, et al., "Direct Binding of Myelin Basic Protein and Synthetic Copolymer 1 to Class II Major Histocompatibility Complex Molecules on Living Antigen-Presenting Cells - Specificity and Promiscuity", Proc. Natl. Acad. Sci. USA, 1994, 91, 4872-4876 **(Exhibit 116)**;

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20, 1994, Herzliya (Israel), 17 **(Exhibit 125)**;

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137. Milo, et al., "Additive Effects of COP-1 and IFN-Beta on Immune Responses to Myelin Basic Protein", Neurol., 1994, 44(Suppl. 2), A212 **(Exhibit 127)**;

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140. Nightingale, et al., "Access to Investigational Drugs for Treatment Purposes", Am. Family Physician, 1994, 50(4), 845-847 **(Exhibit 130)**;

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145. Milo, et al., "Additive Effects of Copolymer-1 and Interferon β-1b on the Immune Response to Myelin Basic Protein", J. Neuroimmunol., 1995, 61, 185-193 **(Exhibit 135)**;

146. O'Connor, et al., "Powders" in The Science and Practice of Pharmacy, Remington, 1995, 2, 1598-1614 **(Exhibit 136)**;

147. Porter, "Coating of Pharmaceutical Dosage Forms," in The Science and Practice of Pharmacy, Remington, 1995, 2, 1650-1659 **(Exhibit 137)**;

148. Reilly, Jr., W.J., "Pharmaceutical Necessities" in The Science and Practice of Pharmacy, Remington, 1995, 2, 1380-1416 **(Exhibit 138)**;

149. Schlegel, et al., "Inhibition of Allorecognition and Prevention of Graft-vs-host Disease (GVHD) by GLAT, a Synthetic Polymer with Promiscuous Binding to Murine and Human

MHC Class II Molecules", in Am. Soc. Hematology, 37th Annual Meeting, Seattle, WA (USA), December 1-5, 1995, 224a (Abstract) **(Exhibit 139)**;

150. Ben-Nun, et al., "The Autoimmune Reactivity to Myelin Oligodendrocyte Glycoprotein (MOG) in Multiple Sclerosis is Potentially Pathogenic: Effect of Copolymer 1 on MOG-induced Disease", J. Neurol., 1996, 243(Suppl. 1), S14-S22 **(Exhibit 140)**;

151. Johnson, Management of Relapsing/Remitting Multiple Sclerosis with Copolymer 1 (Copaxone)", Chemical Abstracts, 1996, 125, 291993b **(Exhibit 141)**;

152. Sykes, "Immunobiology of Transplantation", Faseb J., 1996, 10, 721-730 **(Exhibit 142)**;

153. Teitelbaum, et al., "Copolymer 1 Inhibits Chronic Relapsing Experimental Allergic Encephalomyelitis Induced by Proteolipid Protein (PLP) Peptides in Mice and Interferes with PLP-specific T Cell Responses", J. Neuroimmunol., 1996, 64, 209-217 **(Exhibit 143)**;

154. Aharoni, et al., "Studies on the Mechanism and Specificity of the Effect of the Synthetic Random Copolymer GLAT on Graft-versus-Host Disease", Immunol. Letters, 1997, 58, 79-87 **(Exhibit 144)**;

155. Puri et al., "Modulation of the Immune Response in Multiple Sclerosis", J. Immunol., 1997, 158, 2471-2476 **(Exhibit 145)**;

156. Tarcic et al., "Copolymer 1 (Copaxone) from an Idea to a Drug for Treatment of Multiple Sclerosis" Database HCAPLUS on STN, Israel: AN 1997:333270. Kim, Handasa Kim, 1997, 281(14), 16-18 (Abstract) **(Exhibit 146)**;

157. Teitelbaum, et al., "Copolymer 1 from the Laboratory to FDA", Israel J. Med. Sci., 1997, 33, 280-284 **(Exhibit 147)**;

158. Fridkis-Hareli, et al., "Promiscuous Binding of Synthetic Copolymer 1 to Purified HLA-DR Molecules", J. Immunol., 1998, 160, 4386-4397 **(Exhibit 148)**;

159. Fridkis-Hareli, et al., "Synthetic Amino Acid Copolymers that Bind to HLA-DR Proteins and Inhibit Type II Collagen-reactive T Cell Clones", Proc. Natl. Acad. Sci., October 1998, 95, 12528-12531 **(Exhibit 149)**;

160. Cazzato, et al., "Treatment of Multiple Sclerosis. The Present and the Future. Study Group on Diagnosis and Therapy of Multiple Sclerosis", Database Medline on STN, Instituto do Clinica Neurologica, Universit`a, Trieste, Italy: Medline AN: 2000060325, Recent Progressi in Medicina. October 1999, 90(10), 538-544 (Abstract)**(Exhibit 150)**;

161. Kepsutlu et al., "Evaluation of Chitosan Used as an Excipient in Tablet Formulations", Database HCAPLUS on STN, Department of Pharmaceutical Technology, Gulhane Military Medical Academy, Ankara, 06018, Turkey, HCAPLUS AN: 1999: 590411, Acta. Pol. Pharm. 1999, 56(3), 227-235 (Abstract)**(Exhibit 151)**;

162. Prat, et al., "Lymphocyte Migration and Multiple Sclerosis: Relation with Disease Course and Therapy," Ann. Neurol., 1999, 46: 253-256 **(Exhibit 152)**;

163. Fridkis-Hareli et al., "Synthetic Peptides that Inhibit Binding of the Collagen Type II 261-273 Epitope to Rheumatoid Arthritis-Associated HLA-DR1 and DR4 Molecules and Collagen-Specific T-cell Responses", Database HCAPLUS on STN, Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark, HCAPLUS AN: 2000:455053, Human Immunology, 2000, 61(7), 640-650 (Abstract) **(Exhibit 153)** and

164. Durelli, "Immunotherapeutics of Multiple Sclerosis", Instituto di Clinica delle Malattie del Sistema Nervoso Universita di Torino, 467-475 **(Exhibit 154)**.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required,

authorization is hereby give to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231

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1614

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : Moses Rodriguez and Daren Ure

U.S. Serial No.: 09/885,227 Examiner: Not Yet Known

Filed : June 20, 2001 Group Art Unit: 1614

For : TREATMENT OF CENTRAL NERVOUS SYSTEM DISEASES BY ANTIBODIES AGAINST GLATIRAMER ACETATE

1185 Avenue of the Americas
New York, New York 10036
October 18, 2002



Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT PURSUANT TO 37 C.F.R. §1.97(b)(3)**

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following publications which are listed again on the attached Form PTO-1449 (**Exhibit A**) and copies of References Items 1-47 **(Exhibits 1-44)** are enclosed.

This Supplemental Information Disclosure Statement is being submitted before the issuance of a first Office Action on the merits in connection with the subject application. Accordingly, no fee is required and this Supplemental Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(b)(3).

Applicants also point out that several of the listed references are counterparts of each other and are cumulative. Therefore, in accordance with 37 C.F.R. § 1.98(c), a counterpart of a reference is identified after the cite to the reference, but a copy of only one of the counterparts is being provided. Applicants will provide the Examiner with copies of any reference upon request.

1. U.S. Patent No. 5,554,372, issued September 10, 1996 (Hunter et al.)**(Exhibit 1)**;

2. U.S. Patent No. 5,583,031, issued December 10, 1996 (Stern) **(Exhibit 2)**;

3. U.S. Patent No. 5,623,052, issued April 22, 1997 (McLean et al.) **(Exhibit 3)**;

4. U.S. Patent No. 5,734,023, issued March 31, 1998 (Bishwajit et al.) **(Exhibit 4)**;

5. U.S. Patent No. 5,886,156, issued March 23, 1999 (McLean et al.) **(Exhibit 5)**;

6. U.S. Patent No. 6,362,161, issued March 26, 2002 (Konfino et al.)**(Exhibit 6)**;

7. U.S. Serial No. 09/487,793, filed January 20, 2000 **(Exhibit 7)**;

8. U.S. Serial No. 09/620,216, filed July 20, 2000 **(Exhibit 8)**;

9. U.S. Serial No. 09/765,301. Applicants point out that this reference is a counterpart of PCT International Publication No. WO 01/93893 (PCT/US01/02118)(Exhibit 14);

10. U.S. Serial No. 09/765,644. Applicants point out that this reference is a counterpart of PCT International Publication No. WO 01/52878 (PCT/US01/02117)(Exhibit 13);

11. PCT International Publication No. WO 92/02543 (PCT/EP91/01420), published February 20, 1992 (Gaeta et al.)**(Exhibit 9)**;

12. PCT International Publication No. WO 94/03484 (PCT/US93/06249) published February 17, 1994 (McLean et al.). Applicants point out that this reference is a counterpart of U.S. Patent No. 5,623,052 (Exhibit 3) and U.S. Patent No. 5,886,156 (Exhibit 5);

13. PCT International Publication No. WO 94/26774 (PCT/US94/05632), published November 24, 1994 (Alexander et al.)**(Exhibit 10)**;

14. PCT International Publication No. WO 95/26980 (PCT/US95/04121), published October 12, 1995 (Hackett et al.)**(Exhibit 11)**;

15. PCT International Publication No. WO 95/31997 (PCT/US94/05697), published November 30, 1995 (Reid et al.)**(Exhibit 12)**;

16. PCT International Publication No. WO 01/52878 (PCT/US01/02117), published July 26, 2001 (Eisenbach-Schwartz et al.) **(Exhibit 13)**;

17. PCT International Publication No. WO 01/93893 (PCT/US01/02118), published December 13, 2001 (Eisenbach-Schwartz et al.) **(Exhibit 14)**;

18. Ju et al., "Idiotypic Analysis of Antibodies Against the Terpolymer L-glutamic Acid 60-L-alanine30-L-tyrosine10

(GAT). IV. Induction of CGAT Idiotype Following Immunization with Various Synthetic Polymers Containing Glutamic Acid and Tyrosine", Eur. J. Immunol., 1979, 9(7): 553-560 (Abstract) **(Exhibit 15)**;

19. Schwartz et al., "Gene Complementation in the T Lymphocyte Proliferative Response to Poly (Glu57Lys38Tyr5): Evidence for Effects of Polymer Handling and Gene Dosage", J. Immunol., 1979, 123(1): 272-278 (Abstract) **(Exhibit 16)**;

20. Baxevanis et al., "Genetic Control of T-Cell Proliferative Responses to Poly ($Glu^{40}Ala^{60}$) and Poly ($Glu^{51}Lys^{34}Tyr^{15}$): Subregion-Specific Inhibition of the Responses with Monoclonal Ia Antibodies", Immunogenetics, 1980, 11: 617-628 **(Exhibit 17)**;

21. Maurer et al., "Interpretations of Immune Responses of Mice to Poly(Glu60Lys40), its Modified Derivatives, and the Terpolymers Poly (Glu55Lys37Leu8) and Poly (Glu56Lys37Ser7)", Clin. Immunol. Immunopathol., 1980, 15(3): 344-356 (Abstract) **(Exhibit 18)**;

22. Herzenberg et al., "Lack of Immune Response Gene Control for Induction of Epitope-specific Suppression by TGAL Antigen", Nature, 1982, 295: 329-331 (Abstract) **(Exhibit 19)**;

23. Babu et al., "Reevaluation of Response Patterns of Nonresponder Mice to GlPhe Polymers", Immunogen., 1983, 18(1): 97-100 (Abstract) **(Exhibit 20)**;

24. Babu et al., "Ir Gene Control of T and B Cell Responses to

Determinants in (Glu Lys Ala) Terpolymer", J. Immunogenet., 1984, 11(3-4): 251-254 **(Exhibit 21)**;

25. Falo et al., "Analysis of Antigen Presentation by Metabolically Inactive Accessory Cells and Their Isolated Membranes", Proc. Natl. Acad. Sci. USA, 1985, 82(19): 6647-6651 (Abstract) **(Exhibit 22)**;

26. Trannoy et al., "Epitope-specific Regulation of the T Cell Repertoire: Carrier Recognition in Association with I-E or I-A Does Not Influence the Restriction of Hapten-Specific T Cells", Eur. J. Immunol., 1985, 15(12): 1215-1221 (Abstract) **(Exhibit 23)**;

27. Lai et al., "Complementation of Class II a Alleles in the Immune Response to (Glulystyr) Polymers", Exp. Clin. Immunogenet., 1986, 3(1): 38-48 (Abstract) **(Exhibit 24)**;

28. Lai et al., "Monoclonal T Cell Responses to Two Epitopes on a Single Immunogen Controlled by Two Distinct Genes", J. Immunol., 1986, 136(10): 3799-3804 (Abstract) **(Exhibit 25)**;

29. De Kruyff et al., "Analysis of T Cell Responses to Poly-L (GluLys) at the Clonal Level. I. Presence of Responsive Clones in Nonresponder Mice", Eur. J. Immunol., 1987, 17 (8): 1115-1120 (Abstract) **(Exhibit 26)**;

30. Matsunaga et al., "Complementation of Class II A Alleles in the Immune Response to (Glu-Lys-Tyr) Polymers", Yokohama Med. Bull., 1988, 39(1-2): 9-19 (Abstract) **(Exhibit 27)**;

30. Zisman et al., "Direct Binding of a Synthetic Multichain

Polypeptide to Class II Major Histocompatibility Complex Molecules on Antigen-presenting Cells and Stimulation of a Specific T-cell Line Require Processing of the Polypeptide", Proc. Natl. Acad. Sci. USA, 1991, 88(21): 9732-9742 (Abstract) **(Exhibit 28)**;

31. Deeb et al., "Comparision of Freund's and Ribi Adjuvants for Inducing Antibodies to the Synthetic Antigen (TG)-AL in Rabbits", J. Immunol. Methods, 1992, 152(1): 105-113 (Abstract) **(Exhibit 29)**;

33. Kropshofer et al., "Self-Peptides from Four HLA-DR Alleles Share Hydrophobic Anchor Residues Near the $NH_2$-Terminal Including Proline as a Stop Signal for Trimming", J. Immunol., 1993, 151: 4732-4742 **(Exhibit 30)**;

34. Zisman et al., "Dichotomy Between the T and the B Cell Epitopes of the Synthetic Polypeptide (T,G)-A-L", Eur. J. Immunol., 1994, 24(10): 2497-2505 (Abstract) **(Exhibit 31)**;

35. Asakura and Rodriguez, "A Unique Population of Circulating Autoantibodies Promotes Central Nervous System Remyelination", Multiple Sclerosis, 1998, 4: 217-221 **(Exhibit 32)**;

36. Asakura et al., "Targeting of IgMκ Antibodies to Oligodendrocytes Promotes CNS Remyelination", J. Neurosci., 1998, 18(19): 7700-7708 **(Exhibit 33)**;

37. Li et al., "Glatiramer Acetate Blocks the Activation of THP-1 Cells by Interferon-γ", Eur. J. Pharmacol., 1998, 342: 303-310 **(Exhibit 34)**;

38. Pavelko et al., "Acceleration in the Rate of CNS Remyelination in Lysolecithin-Induced Demyelination", J. Neurosci., 1998, 18(7): 2498-2505 **(Exhibit 35)**;

39. Rodriguez, Neurological Therapeutics, 1998, 15(3): 245-250 **(Exhibit 36)**;

40. Cohen, "Fundamental Immunology", Systemic Autoimmunity, 4th Ed., 1999, 1083 **(Exhibit 37)**;

41. Fridkis-Hareli et al., "Binding of Random Copolymers of Three Amino Acids to Class II MHC Molecules", Intl. Immunol., 1999, 11(5): 635-641 **(Exhibit 38)**;

42. McGavern et al., "Do Antibodies Stimulate Myelin Repair in Multiple Sclerosis", The Neuroscientist, 1999, 5(1): 19-28 **(Exhibit 39)**;

43. Bieber et al., "Antibody-Mediated Remyelination: Relevance to Multiple Sclerosis", Multiple Sclerosis, 2000, 6: S1-S5 **(Exhibit 40)**;

44. Henry, Celia M., "Special Delivery", Chem. and Eng. News, Sept. 18, 2000, 49-54 **(Exhibit 41)**;

45. Warrington et al., "Human Monoclonal Antibodies Reactive to Oligodendrocytes Promote Remyelination in a Model of Multiple Sclerosis", Neurobiology, 2000, 97(12): 6820-6825 **(Exhibit 42)**;

46. Bieber et al., "Humoral Autoimmunity as a Mediator of CNS Repair", Trends in Neurosci., 2001, 24(11): S39-S44 **(Exhibit 43)**; and

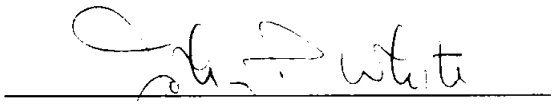
47. Warrington et al., "Immunoglobulin-Mediated CNS Repair", J. Allergy Clin. Immunol., 2001, S121-S125 **(Exhibit 44)**.

Applicants request that the Examiner review the publications and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any fee is required, authorization is hereby give to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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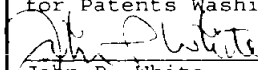

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